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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,883	09/19/2003	Chong-Sheng Yuan	466992001100	6779

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
10/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,883	YUAN, CHONG-SHENG	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/12/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,12,21-23,31-34,37-42,44-48,50-55,58-65 and 67-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,12,21,22,31-34,37-42,44-48,50-55,58-65 and 67-72* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/12/2008 has been entered.

Applicant's cancellation of claims 24-30, amendment of claims 1, 21, 31, 39, 45, 50, 60 and 68, in the paper of 8/12/2008, is acknowledged. Claims 1, 12, 21-23, 31-34, 37-42, 44-48, 50-55, 58-65, 67-72 are still at issue and are present for examination.

Applicants' arguments filed on 8/12/2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claim 23 is objected to because of the following informalities:

Claim 23 depends from rejected claim 1.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 12, 21, 22, 31-34, 37-42, 44-48, 50-55, 58-65, 67-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted that this rejection under 112, first paragraph is similar to that made in the non-final rejection mailed to applicants on 10/18/2007. In response to this previous rejection it is noted that applicants amended the claims to be drawn to a specific chimeric protein and argued the rejection as it applied to the claims to this specific chimeric protein and the rejection was withdrawn based upon applicants amendment of the claims. In response to the final rejection of the claims mailed to applicants on 5/12/2008, applicants have amended the claims to no longer be limited to the specific chimeric proteins previously claimed.

Claims 1, 12, 21, 22, 31-34, 37-42, 44-48, 50-55, 58-65 and 67-72 are directed to all possible chimeric proteins having the enzymatic activity of a nucleotidase, comprising any peptidyl fragment comprising a bacterial leader sequence comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1, any peptidyl fragment that binds to an antibody that specifically binds to an amino acid sequence as set forth in SEQ ID NO: 2 and any peptidyl fragment comprising an amino acid sequence having at least 80% identity with the

amino acid sequence set forth in SEQ ID NO: 1 and methods of methods of their use, encompassed by these claims. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of these enzymes or methods of use of said chimeric protein, by any identifying structural characteristics or properties other than the activity of a nucleotidase, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 12, 21, 22, 31-34, 37-42, 44-48, 50-55, 58-65 and 67-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a chimeric protein having nucleotidase activity comprising the amino acid sequence of SEQ ID NO: 4, does not reasonably provide enablement for any chimeric protein having the enzymatic activity of a nucleotidase, comprising any peptidyl fragment comprising a bacterial leader sequence comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1, any peptidyl fragment that binds to an antibody that specifically binds to an amino acid sequence as set forth

in SEQ ID NO: 2 and any peptidyl fragment comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1 and methods of methods of their use, encompassed by these claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As above, it is noted that this rejection under 112, first paragraph is similar to that made in the non-final rejection mailed to applicants on 10/18/2007. In response to this previous rejection it is noted that applicants amended the claims to be drawn to a specific chimeric protein and argued the rejection as it applied to the claims to this specific chimeric protein and the rejection was withdrawn based upon applicants amendment of the claims. In response to the final rejection of the claims mailed to applicants on 5/12/2008, applicants have amended the claims to no longer be limited to the specific chimeric proteins previously claimed.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1, 12, 21, 22, 31-34, 37-42, 44-48, 50-55, 58-65 and 67-72 are so broad as to encompass any chimeric proteins having the enzymatic activity of a nucleotidase, comprising any peptidyl fragment comprising a bacterial leader sequence comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1, any peptidyl fragment that binds to an antibody that specifically binds to an amino acid sequence as set forth in SEQ ID NO: 2 and any peptidyl fragment comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1 and methods of methods of their use, encompassed by these claims. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of chimeric proteins and methods of use broadly encompassed by the claims. The claims rejected under this section of U.S.C. 112, first paragraph, place minimal if structural limits on the claimed chimeric proteins and methods. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to that 3'(2'),5'-bisphosphate nucleotidase chimeric protein comprising the amino acid sequence of SEQ ID NO: 4.

The specification does not support the broad scope of the claims which encompass any chimeric protein having the enzymatic activity of a nucleotidase, comprising any peptidyl fragment comprising a bacterial leader sequence comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1, any peptidyl fragment that binds to an antibody that specifically binds to an amino acid sequence as set forth in SEQ ID NO: 2 and any peptidyl fragment comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1 and methods of their use, because the specification does not establish: (A) regions of the protein structure which may be modified without nucleotidase activity; (B) the general tolerance of nucleotidases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a 3'(2'),5'-bisphosphate nucleotidase comprising the amino acid sequence of SEQ ID NO: 2 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the 3'(2'),5'-bisphosphate nucleotidase activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the

majority of those chimeric protein having the enzymatic activity of a nucleotidase, comprising any peptidyl fragment comprising a bacterial leader sequence comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1, any peptidyl fragment that binds to an antibody that specifically binds to an amino acid sequence as set forth in SEQ ID NO: 2 and any peptidyl fragment comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1 and methods of methods of their use.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any chimeric protein having the enzymatic activity of a nucleotidase, comprising any peptidyl fragment comprising a bacterial leader sequence comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1, any peptidyl fragment that binds to an antibody that specifically binds to an amino acid sequence as set forth in SEQ ID NO: 2 and any peptidyl fragment comprising an amino acid sequence having at least 80% identity with the amino acid sequence set forth in SEQ ID NO: 1 and methods of methods of their use. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides and methods having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
10/14/2008

/Richard G Hutson, Ph.D./

Primary Examiner, Art Unit 1652